REMARKS

Claims 1, 19, 20, 22, 23, 30, and 35 are pending in the instant application. The rejections set forth in the Office Action have been overcome by argument below.

1. Provisional rejection of claims 1, 19, 20, and 30 for obviousness-type double patenting

The Office Action maintains the provisional rejection of claims 1, 19, 20, and 30 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 56-68 of U.S. Application No. 11/452,434 (the '434 application)[1]. The Action states that while the conflicting claims are not identical, they are not patentably distinct from each other because claims 56-64, 80, and 81 of the '434 application recite "[a] trimeric polypeptide complex comprising three monomer polypeptides, wherein (i) each of said monomer polypeptides comprises a tetranectin trimerising structural element (TTSE), said TTSE being a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40 and (ii) at least one of said monomer polypeptides is covalently linked to at least one heterologous moiety, where said at least one heterologous moiety is different from any of the fusion proteins CIIH6FXTN123, H6FXTN123, H6FXTN12, H6FXTN23, the sequences of which are shown in SEQ ID NOs:24-27, and said complex remains as a trimer at a temperature of at least 60°C." The Action also states that the rejection is maintained for reasons of record set forth at pages 9-11 of the Office action mailed August 22, 2008 pages 14-16 of the Office Action mailed February 12, 2009, and pages 10-12 of the Office Action mailed July 24, 2009.

The Action mailed August 22, 2008 asserts that the claims of the instant application and the '434 application are not patentably distinct from each other because the claims of the instant application encompass a trimeric polypeptide comprising three monomers, wherein each monomer comprises a cytokine binding member domain and a tetranectin trimerising domain, and thus, encompass subject matter that is a species of the claimed subject matter of the '434 application. The Action mailed August 22, 2008 also asserts that in view of the '434 application, the trimeric

[1] Applicants note that the '434 application issued as U.S. Patent No. 7,642,044 ("the '044 patent") on January 5, 2010.

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polypeptides of the instant application would have been obvious to one of ordinary skill in the art at the time the present invention was made. The Actions mailed February 12, 2009 and July 24, 2009 simply refer to the discussion in the Action mailed August 22, 2010.

An obviousness-type double patenting rejection is appropriate where any claim in an examined application defines an invention that is an obvious variation of an invention claimed in a commonly owned patent. M.P.E.P. § 804. An obviousness-type double patenting rejection is analogous to a failure to meet the nonobviousness requirement of 35 U.S.C. § 103, with the exception that the patent underlying the double patenting rejection is not considered prior art. *Id.* Thus, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of an obviousness determination and includes the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1 (1966). *Id.* In the context of an obviousness-type double patenting analysis, these factual inquiries include: (1) determining the scope and content of a patent claim relative to a claim in the application at issue; (2) determining the differences between the scope and content of the patent claim and the claim in the application at issue; (3) determining the level of ordinary skill in the pertinent art; and (4) evaluating any objective indicia of nonobviousness (such as evidence of commercial success, long felt but unsolved need, failure of others, unexpected results, and copying). *Id.*

Because an obviousness-type double patenting analysis parallels an obviousness analysis, the guidelines for analyzing an application for compliance with 35 U.S.C. § 103 may be used when conducting an obviousness-type double patenting analysis. Thus, when conducting an obviousness-type double patenting analysis, a factfinder must be aware of the distortion caused by hindsight bias and be cautious of arguments reliant upon *ex post* reasoning. *KSR Int'l Co.*, 127 S. Ct. at 1742; *Sanofi-Synthelabo v. Apotex,* 550 F.3d 1075, 1088 (citing *KSR Int'l Co.* for the proposition that hindsight reasoning is inappropriate in determination of obviousness). Moreover, when the prior art teaches away from combining certain known elements, the combination of such elements is more likely to be nonobvious. *Id.* at 1740; *Anderson Corp. v. Pella Corp.*, 300 Fed. Appx. 893, 898 (Fed. Cir. 2008) (noting that the teaching-away evidence presented by the applicant would have arguably discouraged an ordinarily skilled artisan from making the claimed combination). In addition, it is a

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long-standing tenet of patent law that a species is nonobvious over a prior art genus, where the prior art reference disclosing the genus does not teach or suggest the selection of the species. *In re Baird,* 16 F.3d 380 (Fed. Cir. 1994).

Applicants respectfully disagree with the Action's assertion that in view of the '434 application, the trimeric polypeptides of the instant application would have been obvious to one of ordinary skill in the art at the time the instant invention was made. Applicants contend that because bivalent antagonists of the TNF superfamily were well known at the time the instant application was filed, it would not have been obvious to one of ordinary skill in the art to make the claimed trimeric polypeptides comprising a TNF receptor and tetranectin trimerising structural element (TTSE). For example, at the time the instant application was filed, two TNF antagonists – infliximab and etanercept – were approved for the treatment of arthritis. Scallon *et al.*, *J Pharmacol Exp Ther.* 301(2): 418-26, 418 (2002). These molecules fundamentally differ with regard to their molecular structures, binding specificities, and manner in which they neutralize TNF. *Id.*

With regard to their molecular structures, infliximab is a chimeric monoclonal antibody with murine variable regions and human IgG1 and κ constant regions, and etanercept is a fusion protein consisting of the extracellular domain of the p75 TNF receptor and the hinge and Fc domains of human IgG1. *Id.* Thus, neither of these molecules is trivalent. As for their binding specificities, the bivalent infliximab molecule is capable of binding two TNF molecules, and up to three infliximab molecules can bind a single TNF homotrimer thereby blocking all TNF receptor binding sites. *Id.* at 419. In contrast, Scallon *et al.* note that the bivalent etanercept molecule likely forms a 1:1 complex with the TNF trimer in which two of the three TNF receptor binding sites are occupied and the third is open. *Id.* Scallon *et al.* also note that infliximab forms more stable complexes with both soluble TNF (sTNF) and the transmembrane form of TNF (tmTNF). *Id.* at 418. Notwithstanding the fact that infliximab has been shown to be more effective than etanercept at neutralizing tmTNF, it is clear that both molecules are bivalent and that both molecules have been effective in providing symptomatic improvement and inhibition of structural damage progression in rheumatoid arthritis patients. *Id.* at 424. Absent Applicants teachings regarding trimeric (*i.e.*, trivalent) polypeptides comprising three monomers that further comprise a member of the TNF superfamily, one of ordinary

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skill in the art would have looked to the teachings of Scallon *et al.*, which show that two structurally distinct molecules effectively bind sTNF and tmTNF.

In view of the teachings of Scallon *et al.*, in which bivalent TNF antagonists having different structures and binding specificities were shown to be effective in neutralizing TNF, one of ordinary skill in the art would not have believed that there was a "known problem for which [the instant invention] was an obvious solution." *KSR Int'l Co.*, 127 S. Ct. at 1742 ("When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense."). In fact, because two bivalent molecules had been shown to be effective as TNF antagonists – and infliximab and etanercept were sufficiently effective to have enjoyed commercial success – Applicants contend that the valency of a molecule did not present a problem that needed to be resolved before effective TNF antagonists could be developed. In other words, it would not have been obvious to one of ordinary skill in the art at the time the instant application was filed to make the claimed trimeric polypeptides.

Applicants also disagree with the Action's assertion that the instant claims encompass subject matter that is a patentably indistinct species of the claimed subject matter of the '434 application. Claim 1 of the instant application (from which claims 19, 20, and 30 depend) recites "[a] trimeric polypeptide comprising three monomers, wherein a first portion of each monomer comprises TNFRSF1A, TNFRSF1B, LTBR, TNFRSF4, TNFRSF5, TNFRSF6, TNFRSF6B, TNFRSF7, TNFRSF8, TNFRSF9, TNFRSF10A, TNFRSF10B, TNFRSF10C, TNFRSF10D, TNFRSF11A, TNFRSF11 B, TNFRSF12, TNFRSF12L, TNFRSF13B, TNFRSF13C, TNFRSF14, NGFR, TNFRSF17, TNFRSF18, TNFRSF19, TNFRSF19L, TNFRSF21, TNFRSF22, or TNFRSF23, and a second portion of each monomer is a tetranectin trimerising structural element comprising an amino acid sequence having at least 87% identity with the amino acid sequence of SEQ ID NO:81." Therefore, while the claims of the '434 application are directed to trimeric polypeptide complexes comprising three monomer polypeptides that further comprise a tetranectin trimerising structural element (TTSE) covalently linked to at least one heterologous moiety, the monomer polypeptides of claim 1 of the instant application comprise specifically recited members of the TNF superfamily,

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namely, the receptors TNFRSF1A, TNFRSF1B, LTBR, TNFRSF4, TNFRSF5, TNFRSF6, TNFRSF6B, TNFRSF7, TNFRSF8, TNFRSF9, TNFRSF10A, TNFRSF10B, TNFRSF10C, TNFRSF10D, TNFRSF11A, TNFRSF11 B, TNFRSF12, TNFRSF12L, TNFRSF13B, TNFRSF13C, TNFRSF14, NGFR, TNFRSF17, TNFRSF18, TNFRSF19, TNFRSF19L, TNFRSF21, TNFRSF22, and TNFRSF23.

For the purpose of rebutting the double patenting rejection, Applicants submit that the specifically recited members of the TNF superfamily in claim 1 are patentable species over the genus of heterologous moieties recited in the '434 application. While the '434 application suggests that a heterologous moiety can be a cytokine such as an interferon or a leukotriene (the '044 patent, col. 9, ln. 54 to col. 10, ln. 5), the '434 application does not suggest that a heterologous moiety can be a trimeric cytokine. Pursuant to *Baird*, where a reference does not provide any suggestion to select a particular species encompassed by its generic disclosure, that species remains nonobvious over the generic disclosure. *In re Baird*, 16 F.3d 380 (Fed. Cir. 1994). With respect to the instant case, the genus of heterologous moieties recited in the '434 application is large, the '434 application does not suggest trimeric cytokines, the art is unpredictable, there is a lack of a reasonable expectation of success, and the art teaches away from the claimed invention.

For the reasons discussed herein, Applicants submit that the subject matter of claims 1, 19, 20, and 30 is not an obvious variation of the invention claimed in the '434 application. Applicants, therefore, respectfully request that the double-patenting rejection over the '434 application be withdrawn.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Mertz believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

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Respectfully submitted,
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